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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/903,508	07/13/2001	Charles Abbas	1533.0830003/MAC/RGM	3856

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STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER
LAMBERTSON, DAVID A

ART UNIT	PAPER NUMBER
1636	17

DATE MAILED: 06/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/903,508	ABBAS ET AL.	
	Examin r	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *22-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt is acknowledged of a reply, filed April 16, 2003 as Paper No. 16, to the written Restriction Requirement mailed December 17, 2002 as Paper No. 13..

Claims 1-31 are pending in the instant application. Claims 1-21 are ready for examination in the instant application. Claims 22-31 are withdrawn as being drawn to a non-elected invention with traverse.

Election/Restrictions

Applicant's election with traverse of Group I in Paper No. 17 is acknowledged. The traversal is on the ground(s) that (a) the subject matter of each of the groups is overlapping and therefore does not present an undue search burden; (b) that because Group II represents mutant yeasts that have been generated from the yeasts of Group I, the inventions are the same and should be examined together. This is not found persuasive because of the following reasons (set forth as they correspond to the grounds of traversal in a point-by-point manner, for applicant's ease):

A. The fact that the subject matter overlaps is not sufficient grounds for rejoinder. The scope of the claims must be commensurate in order for there to be no burden of search. In the instant case, although the yeast strains of Group I can be used to make the yeast strains of Group II, the yeast strains of Group II are very different from those of Group I in that they comprise different mutations. As a result, these strains have different genetic backgrounds, each with different characteristics (for instance, with regard to their ability to produce riboflavin in a particular medium). Additionally, riboflavin can be isolated from yeasts other than those disclosed in the

instant specification, thus methods of obtaining riboflavin are also patentably distinct from the strains of Group I.

B. Furthermore, the *rib* mutant strains indicated in Group II can be obtained using strains that are not present in Group I. Therefore, although the subject matter of both groups may overlap, the scopes are not commensurate by the fact that art regarding Group I does not necessarily produce art regarding Group II, and *vice versa*. The fact that one yeast was produced using the other is not a method of using the two yeasts together; rather it is a method of using one yeast to make the other (e.g., a product and process of making, which is another method of establishing independent inventions). Since the claims are directed to the yeast, and not the method of making the yeast (it is noted that the transformation process claims have been included with the ARS element claims), these claims are unrelated as set forth in the Election/Restriction requirement because the restriction was performed with regard to the yeast strain claims of Group I. However, from the perspective of the transformation (e.g., method) claims of Group I, one could easily indicate that the methods could be used to make an entirely different product, such as a yeast with a mutation in a non-*rib* gene. Therefore, it is the examiner's contention that the inventions are still patentably distinct in view of applicant's arguments.

The requirement is still deemed proper and is therefore made FINAL.

Priority

Applicant's claim for domestic priority to provisional application US 60/218,244 under 35 U.S.C. 119(e) is acknowledged.

Information Disclosure Statement

The information disclosure statement filed December 17, 2002 has been considered, and a signed and initialed copy of the form PTO-1449 has been attached to this Office Action.

In addition, the examiner noticed that there was an IDS filed July 18, 2002. However, several attempts to locate the references within the Office have been unsuccessful. Rather than return a 16 page PTO-1449 completely crossed out, the examiner hopes that this information will prompt applicant to resubmit the references for consideration along with a response to this Office Action. An electronic filing, as performed with the December 17, 2002 filing, would be favorable. The examiner apologizes for any inconvenience this has caused.

Claim Objections

Claims 1-21 are objected to because of the following informalities: the claims are directed to non-elected subject matter, specifically SEQ ID NO: 1 and 2. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the strains ATCC 9058 and NRRL Y-30292 are required to practice the invention (for the purpose of obtaining library segments therefrom, and transforming the strains with the ARS sequence). As such, the strains must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the strains. In the instant case, the process to generate the strains that is disclosed in the specification does not appear to be repeatable, nor does it appear the strains are readily available to the public.

> If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that:

a) during the pendency of the application, access to the invention will be afforded to the Commissioner upon request;

b) all restrictions upon availability to the public will be irrevocably removed upon the granting of the patent;

c) the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request for the enforceable life of the patent, whichever is longer;

d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and

e) the deposit will be replaced if it should ever become inviable.

It is noted that strain NRRL Y-30292 has been deposited under the Budapest Treaty. However, there is no statement or declaration that the strain will be irrevocably and without restriction released to the public upon the issuance of a patent. There is no clear indication of a deposit for ATCC 9058.

Failure to make one of the preceding indications in response to this Office Action will result in the rejection being maintained in either a second Non-Final or a Final rejection.

If an applicant can adequately establish that a biological material is known and readily available, the Office will accept that showing. In those instances, however, the applicant takes the risk that the material may cease to be known and readily available. Such a defect cannot be cured by reissue after the grant of a patent. On the other hand, Ex parte Humphreys, 24 USPQ2d 1255 (Bd. Pat. App. & Int. 1992), held that the only manner in which applicants could satisfy their burden of assuring public access to the needed biological material, and, thereby, compliance with the enablement requirement of 35 U.S.C. 112, was by making an appropriate deposit. Those applicants that rely on evidence of accessibility other than a deposit take the risk that the patent may no longer be enforceable if the biological material necessary to satisfy the requirements of 35 U.S.C. 112 ceases to be accessible. See MPEP § 2404.01.

Claims 1-14, 20 and 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims an isolated polynucleotide comprising an ARS sequence having at least 95% sequence identity to SEQ ID NO: 3 of the instant specification. The claims read on a broad genus of sequences that are 95% similar to SEQ ID NO: 3 that may or may not have the ability to function as an ARS element. Furthermore, there is no indication as to in what type of cells the sequences are able to function as an ARS element.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the instant case, the specification does not sufficiently describe a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics.

Applicant claims a sequence having 95% sequence identity to SEQ ID NO: 3 and having the ability to function as an ARS element by function only, without any disclosed or known correlation between the elements and their function. The specification only provides teachings regarding the use of SEQ ID NO: 3 as an ARS element in *Candida famata*. The specification does not teach modifications can be made to SEQ ID NO: 3 and still have it function as an ARS element. Furthermore, the specification does not teach the types of cells in which SEQ ID NO: 3, even as unmodified, can function as an ARS element; this is an important functional limitation of the sequence as set forth in the claim and the specification. It is well established in the prior art that, although it is clear that many types of cells have ARS elements, there is no consensus

sequence which would allow the skilled artisan to identify an ARS element by sequence homology (see for example Clyne et al., Methods 13: 221-233; see entire document, especially page 225, right column, second and third full paragraphs). This is evidenced by the fact that the ARS elements that have been characterized in two types of yeast, *S. cerevisiae* and *S. pombe*, have no sequence element that is common to all such ARS elements. Furthermore, Clyne et al. teaches that although a variety of ARS elements have been isolated from different organisms, they have not been shown to function as ARS elements even in the organisms from which they are derived, probably as a result of their inability to bind to specific replication proteins (see for example page 225, right column, second and third full paragraphs). The skilled artisan cannot envision a sufficient number of embodiments of the instant invention from the instant specification because the specification only discloses the use of one sequence, SEQ ID NO: 3, in one type of organism, *Candida famata*, and the prior art teaches the unpredictability of predicting ARS functionality by sequence homology, as well as across different organisms.

The prior art does not provide sufficient information on the subject to overcome the deficiencies of the instant specification. In fact, as indicated above, the prior art indicates the unpredictable nature of using a particular ARS element across species, and the inability to predict ARS function as a result of sequence homology. Thus the skilled artisan cannot rely on the prior art to envision a sufficient number of embodiments of the instant invention to see that the applicant was in possession of the claimed genus. This includes which sequences that are 95% identical to SEQ ID NO: 3 which can function as ARS elements, and which cells can be transformed with the ARS elements so that the ARS elements are functional.

Neither the specification of the instant application or the prior art teaches a structure-function relationship for a representative number of sequences which can function as ARS elements in a representative number of different host cells. As a result, the skilled artisan would not be able to envision the claimed invention by relying on the teachings of the prior art or the instant specification. Therefore applicant has not satisfied the written description requirement to show the skilled artisan that they were in possession of the claimed genus.

Claims 15-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for electroporating *Candida famata*, does not reasonably provide enablement for any yeast strain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) the most relevant of which are discussed below:

Nature of the invention. The nature of the invention is a method of transforming any type of yeast cell by exposing the cell to a particular strength electrical field, specifically between 8 and 15 kV/cm.

Scope of the invention. The scope of the invention is very broad, encompassing the ability to transform all types of yeast using this particular rage of field strengths.

State of the art. The state of the art indicates that a typical field strength for the transformation of yeast is 2.5-4.5 kV/cm. This is evident in Raymond et al. (US Patent No. 5,854,039; see entire document; henceforth Raymond), throughout the specification (in particular, see the Abstract).

Number of working examples and Guidance provided by applicant. The instant specification clearly indicates the ability to electroporate Candida famata using a field strength of 8-15 kV/cm. However, there is no indication that this field strength would be sufficient or acceptable for the transformation of all types of yeast. The specification does not address the potential dangers of using the particular range on any type of yeast, other than Candida famata. Such dangers include affecting the viability or performance of the yeast in assays, as well as potential loss of DNA sample resulting from the obliteration of the cell under a particular field strength..

Level of skill in the art. The level of skill in the art, using the particular field strength recited in the claim, is underdeveloped, indicated by the fact that typical field strengths for the electroporation of yeast, as taught by Raymond, is from 2.5-4.5 kV/cm.

Unpredictability of the art. The art is highly unpredictable. There is no information suggesting that a field strength of 8-15 kV/cm is applicable to all types of yeast, wherein the yeast will be transformed with a reasonable expectation of success. In fact, the art appears to teach away from such a suggestion because Raymond describes an ideal field strength of 2.5-4.5 kV/cm, which is significantly lower than the range suggested in the instant specification. When

practicing the claimed invention, the skilled artisan would be practicing undue and unpredictable trial and error experimentation by using the field strength of the instant invention, because the skilled artisan could not reasonably predict that their cells would respond to the particular field strength and be effectively transformed or whether the cells would actually survive the particular field strength of 8-15 kV/cm. As a result, the skilled artisan takes the risk of losing potentially valuable DNA samples and valuable time waiting for a transformation to occur which may or may not be obtainable.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 19 is rejected under 35 U.S.C. 102(b) as being anticipated by Raymond et al. (US Patent No. 5,854,039; see entire document; henceforth Raymond).

The examiner would like to indicate that claim 19 as it currently reads is directed to a method of electroporation for yeast cells, wherein yeast is a broad genus of organisms. Raymond teaches a method of transforming the yeast *Pichia methanolica* (see for example the Abstract) using a cell suspension of said yeast cells together with DNA molecules, such as expression cassettes that contain promoter and terminator elements and a gene of interest (see for example column 4, lines 51-56). The transformation method involves electroporation of the cells, which have been washed in an electroporation buffer which comprises sucrose (see for

example column 7, lines 20-23). Therefore, Raymond meets all of the limitations of the instant claim.

Allowable Subject Matter

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson
June 27, 2003

PATENT EXAMINER
Gerald G. Letters Jr
A.U. 1636